
7

Letter to the Editor

The role of radiotherapy in the treatment of non-functioning pituitary adenomas

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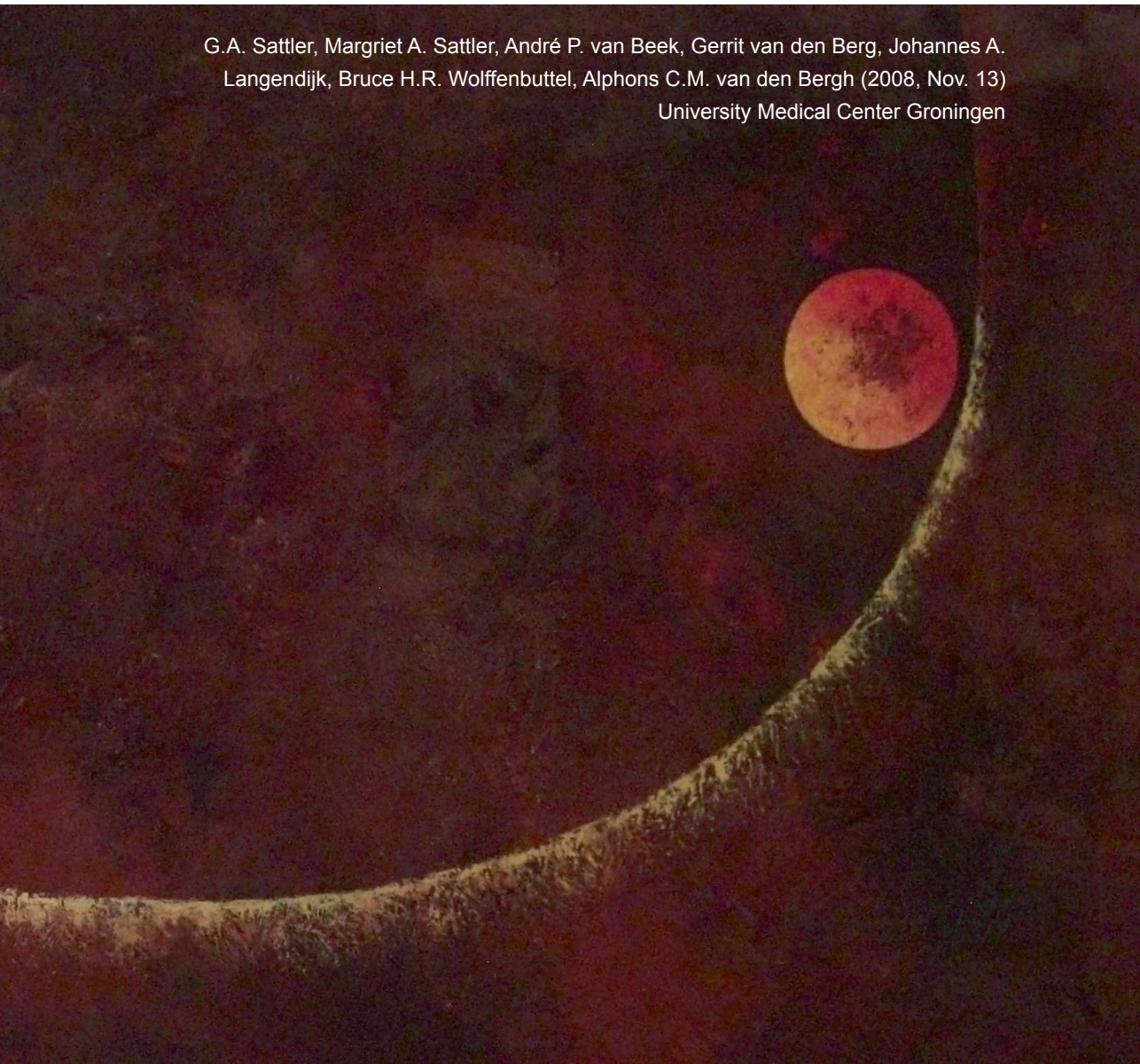

TO THE EDITOR

With great interest we read the manuscript of Dekkers et al., who reviewed the literature on treatment and follow-up of non-functioning pituitary macroadenomas (NFA) [1].

The authors concluded that appropriate tumor control can be achieved after neurosurgery without radiotherapy in the majority of NFA patients. Moreover, they concluded that salvage radiotherapy is effective in stabilizing tumor growth in residual disease, and that postoperative radiotherapy is associated with long-term side effects in the absence of any benefits to long term tumor control.

We strongly feel that there is insufficient data to support these conclusions. First, including only series with patients mainly treated by transsphenoidal surgery in the review, creates the wrong impression that the 10 year progression-free survival without radiotherapy is 50-79%, as reported in the review by Dekkers et al. [1]. In fact, in daily clinical practice, a substantial portion of the NFA patients requires bulk resection by craniotomy. Moreover, the outcome of surgery is determined by the surgeon's experience, which may differ widely among centers. A more realistic description on 10 year progression free survival after surgery without radiotherapy with longer follow-up time was reported to be 47% [2], and 22 % [3]. In comparison, in the study by Van den Bergh et al. the 10 year progression free survival after surgery with immediate post-operative radiotherapy was 95% [3]. This excellent local control was reported by several other study groups [2,4].

Second, the authors stated that in case of regrowth in residual disease, salvage radiotherapy remains effective in stabilizing tumor growth or in inducing regression of the pituitary tumor. They advocate this wait- and see policy based on one paper by Park et al.. However, in this study, 50.5% developed a recurrence within 10 years compared to 2.3% among those treated with immediate postoperative radiotherapy [4]. Given the natural history of these tumors, it is very likely that a longer follow-up time will further increase these recurrence rates. A wait-and see policy can be expected to result in more frequent MRI investigations, and an increased frequency of re-operations with its associated peri-operative mortality risk. In the study by Park et al., 23% of patients with recurrence in the observation group were lost to follow up and all presented with symptomatic recurrent disease, necessitating a second operation in most of them [4].

Third, concerns about long-term side-effects of radiotherapy are often cited to delay or reject this treatment. Radiotherapy might act as a risk factor for cerebrovascular disease, but available epidemiological studies discussed in the review by Erfurth et al. do not provide evidence to consider pituitary radiotherapy as a stronger risk factor compared to other risk factors in pituitary adenoma patients [5]. Furthermore, our group reported that the natural course of the extent and timing of pituitary deficiencies in patients who received immediate postoperative radiotherapy did not differ from those who did not receive radiotherapy [3]. In

addition, a study by Erfurth et al. gave no firm support for an increased incidence of secondary brain tumors in patients with pituitary adenomas treated with surgery and radiotherapy [6]. The two studies cited in the manuscript of Dekkers et al. reported an increased cumulative risk for brain tumors after radiotherapy. However, these studies do not provide sound evidence that radiotherapy per se is the causal factor because the comparison with regard to the incidence of brain tumors were made with the general population instead of non-irradiated pituitary patients.

Fourth, our group also reported that optic nerve atrophy is a rare long-term complication of radiotherapy with an overall incidence of 0.5% with a follow-up of at least 18 months [7]. It is expected that the incidence will decline with modern radiotherapy equipment and current recommended radiotherapy doses.

Finally, we and other authors including Dekkers et al. have convincingly shown that postoperative radiotherapy in patients with NFA was not associated with reduced quality of life or cognition when compared to surgery alone [8].

These findings favor the use of radiotherapy in NFA patients with residual disease rather than the highly restrictive recommendations made by Dekker and coauthors. Radiotherapy should therefore not be denied as an important therapeutic modality to this particular group of patients who can benefit from it.

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